

Remarks

Introduction

Claims 25-31 were pending. By way of this response, claims 25-31 have been amended. Support for the amendments to the claims can be found in the specification as filed, and care has been taken to avoid adding new matter. Accordingly, claims 25-31 remain pending.

Claim Objections

Claims 25 and 28 have been objected to for various informalities.

Claims 25 and 28 have been amended as set forth above. Applicant submits that in view of the amendments to the claims, the objections have been overcome.

Obviousness-Type Double Patenting

Claims 25, 27, and 31 have been rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 2-5, 9, 12-14, 24, 28, and 31 of U.S. Patent No. 6,787,517.

Applicant disagrees with the rejections. In addition, applicant submits that in view of the amendments to the claims set forth above, the rejection has been overcome.

Claim 1 of U.S. Patent No. 6,787,517 discloses an agent that comprises a therapeutic component and a targeting ligand

that is effective to bind to the alpha-2B or alpha-2B/alpha-2C adrenergic receptor subtypes.

The present claims are directed to compositions which comprise a soluble recombinant botulinum toxin protein. The soluble recombinant botulinum toxin protein comprises a C-terminal portion of a botulinum toxin which includes a botulinum toxin receptor binding domain. Therefore, the soluble recombinant botulinum toxin protein of the present compositions includes a portion effective to bind to botulinum toxin receptors. Thus, the botulinum toxin proteins of the present compositions are different and distinct from an agent which comprises a targeting ligand that binds to adrenergic receptors, as claimed in U.S. Patent No. 6,787,517.

In view of the above, applicant submits that the present claims are unobvious from and patentable over the claims of U.S. Patent No. 6,787,517, and requests that the double patenting rejection be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 25-31 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. In particular, the claims have been rejected for the use of the term "portions".

Independent claim 25 has been amended as set forth above. Applicant traverses the rejection as it relates to the present claims.

Claim 25 has been amended to make more clear that the C-terminal portion of the botulinum toxin heavy chain includes the botulinum toxin receptor binding domain.

In view of the amendments to claim 25, applicant submits that the term portion in the claims does not read on a single amino acid, and that the present claims are definite.

In view of the above, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejection Under 35 U.S.C. § 102

Claims 25-26 and 29-31 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Whelan et al. (1992). Claims 25-26 and 29-31 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Campbell et al. (1997). Claims 25-26 and 28 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Maisey et al. (1988). Claims 25-29 and 31 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Dolly et al. (U.S. Patent No. 6,203,794). Claims 25-31 have been rejected under 35 U.S.C. § 102(a) as allegedly being anticipated by WO 94/21684.

Applicant traverses each of the rejections as it pertains to the present claims.

Whelan et al. discloses the nucleotide sequence of botulinum toxin type B. Importantly, Whelan only discloses the

predicted amino acid sequence of botulinum toxin types A, B, C, D, and E (e.g., see FIG. 4, and page 2348 right column). Whelan does not disclose an actual botulinum toxin protein, let alone, a botulinum toxin protein provided as a component of a composition.

Applicant notes that the Office Action indicates that Campbell et al. has a publication date of 1997. Upon review of Campbell et al., it appears that Campbell et al. has a publication date of 1993 based on the publication in Biochim. Biophys. Acta 1216:487-491. Campbell et al. discloses the nucleotide sequence of botulinum toxin type G. Campbell et al. appears to disclose the predicted amino acid sequence of botulinum toxin type G. Campbell et al. does not disclose an actual botulinum toxin protein, let alone, a botulinum toxin protein provided as a component of a composition.

Maisey et al. discloses botulinum toxin types A and B purified from cultures of the anaerobic bacteria Clostridium botulinum. Maisey et al. does not disclose, teach, or even suggest a recombinant botulinum toxin protein comprising a C-terminal portion of a heavy chain of a botulinum toxin produced in soluble form in aerobic bacteria and obtained therefrom without Clostridium botulinum neurotoxin complex proteins.

Dolly et al. discloses a recombinantly produced botulinum toxin light chain coupled to a native botulinum toxin heavy chain (i.e., a botulinum toxin heavy chain obtained from anaerobic Clostridium botulinum bacteria). More specifically, Dolly et al. discloses a fusion protein which comprises a botulinum toxin light chain coupled to a maltose binding protein

(MBP). Dolly et al. does not disclose, teach, or even suggest a recombinant botulinum toxin protein comprising a C-terminal portion of a heavy chain of a botulinum toxin produced in soluble form in aerobic bacteria and obtained therefrom.

WO 94/21684 discloses the use of a botulinum toxin fragment less than 35 amino acid residues and without botulinum toxin activity as a vaccine for botulinum toxin poisoning. The botulinum toxin fragment disclosed by WO 94/21684 does not include a botulinum toxin receptor binding domain. In addition, WO 94/21684 does not disclose, teach, or even suggest a soluble recombinant botulinum toxin protein which comprises a C-terminal portion of the heavy chain of a botulinum toxin serotype selected from the group consisting of botulinum toxin types B, C1, D, E, F and G, which portion includes a botulinum toxin receptor binding domain.

Applicant submits that neither Whelan et al. nor Campbell et al. disclose, teach, or suggest the present invention. For example, neither Whelan et al. nor Campbell et al. disclose, teach, or even suggest a composition comprising a soluble recombinant botulinum toxin protein, let alone, a soluble recombinant botulinum toxin protein, as recited in claim 25.

As discussed above, both Whelan et al. and Campbell et al. disclose predicted amino acid sequences. Thus, neither Whelan et al. nor Campbell et al. disclose each and every element recited in the present claims. This is supported by the indication in the Office Action that claim 28, which is directed to a botulinum toxin protein in solution, is not anticipated by either Whelan et al. or Campbell et al.

Maisey et al. does not disclose, teach, or suggest the present invention. For example, Maisey et al. does not disclose, teach, or even suggest a composition comprising a soluble recombinant botulinum toxin protein, which comprises a soluble C-terminal portion produced in soluble form in aerobic bacteria and obtained therefrom. As discussed above, Maisey discloses the use of botulinum toxin types A and B as obtained from anaerobic Clostridial bacteria. The toxins disclosed by Maisey are produced with associated Clostridial botulinum neurotoxin complex proteins. Therefore, applicant submits that the present compositions and the compositions disclosed by Maisey et al. are different and distinct, one from the other. Thus, applicant submits that Maisey et al. does not teach each and every element recited in the present claims, and therefore does not anticipate the present claims.

Dolly et al. does not disclose, teach, or suggest the present invention. For example, Dolly et al. does not disclose, teach, or even suggest a composition comprising a soluble recombinant botulinum toxin protein which comprises a soluble C-terminal portion of a botulinum toxin heavy chain which is soluble in aerobic bacteria.

As discussed above, Dolly et al. discloses the use of MBP in the formation of a recombinant light chain of a botulinum toxin. The present claims are directed to compositions comprising the C-terminal portion of a heavy chain of a botulinum toxin. Thus, applicant submits that the compositions disclosed by Dolly et al. and the presently claimed compositions are different and distinct, one from the other. Thus, applicant

submits that Dolly et al. does not disclose, teach, or even suggest each and every element recited in the present claims, and therefore, does not anticipate the present claims.

WO 94/21684 does not disclose, teach, or suggest the present invention. For example, WO 94/21684 does not disclose, teach, or even suggest a composition comprising a soluble recombinant botulinum toxin protein which comprises a C-terminal portion of a botulinum toxin heavy chain, which includes a botulinum toxin receptor binding domain. As discussed in paragraph [0102] of the above-identified patent application, the botulinum toxin receptor binding domain encompasses several hundred amino acids. In contrast, WO 94/21684 discloses a botulinum toxin fragment of less than 35 amino acids. Thus, applicant submits that the soluble recombinant botulinum toxin protein of the present compositions is structurally different and distinct from the botulinum toxin fragment of WO 94/21684. Therefore, applicant submits that WO 94/21684 does not disclose, teach, or even suggest each and every element recited in the present claims, and therefore, does not anticipate the present claims.

In view of the above, applicant submits that the present claims, that is claims 25-31, are not anticipated by Whelan et al., Campbell et al., Maisey et al., Dolly et al., or WO 94/21684, under 35 U.S.C. § 102.

In addition, applicant submits that the present claims, that is claims 25-31, are unobvious from and patentable over any of the prior art, taken alone or in any combination, under 35 U.S.C. § 103.

For example, the references, Whelan and Campbell do not even suggest an actual protein present in a composition since the disclosure of Whelan and Campbell are limited to predicted amino acid sequences. As understood by persons of ordinary skill in the art, predicted amino acid sequences do not provide information other than the primary amino acid sequence of a protein. For example, predicted amino acid sequences fail to take into account other features, such as tertiary structures, of proteins, and the like, that are associated with actual proteins.

Maisey fails to disclose, teach, or even suggest any botulinum toxin protein that is obtained from aerobic bacteria, let alone obtained without Clostridium botulinum toxin complex proteins. Since the compositions of Maisey do not comprise a botulinum toxin protein obtained from aerobic bacteria, Maisey does not suggest the presently claimed invention.

Dolly and WO 94/21684 disclose proteins other than those recited in the present claims. For example, Dolly discloses proteins comprising a recombinant botulinum toxin light chain and WO 94/21684 discloses peptides with less than 35 amino acid residues. Dolly and WO 94/21684 do not even suggest a soluble recombinant botulinum toxin protein which comprises a C-terminal portion of a heavy chain of a botulinum toxin, which portion includes a botulinum toxin receptor binding domain, as recited in the present claims.

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of